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DIAGNOSTIC ACCURACY OF CONTRAST-ENHANCED MAMMOGRAPHY VERSUS BREAST MRI IN BREAST CANCER DETECTION: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Breast cancer is the most frequently diagnosed form of cancer among women, and a primary source of cancer related death globally. Contrast-enhanced magnetic resonance imaging (MRI) of the breast is considered the most sensitive method of detecting breast cancer by medical imaging at this time, but its high cost, long acquisition time, limited availability in certain areas, and various contraindications (e.g., metal implants) hinder its routine application. Contrast-enhanced mammography (CEM) has emerged as an alternative to MRI for breast cancer detection that allows for faster and more accessible detection of breast cancer with simultaneous acquisition of both morphology and function in one examination.

Objective: The purpose of this study was to conduct a systematic review and comparison of the diagnostic performance of CEM with that of contrast-enhanced breast MRI for the detection of breast cancer in adult women with regard to sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Methods: We performed a systematic review of the literature on the comparison of contrast-enhanced mammography (CEM) and magnetic resonance imaging (MRI) as imaging modalities used to evaluate breast cancer. Our review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. We included original studies that directly compared CEM and MRI in the same patient cohort with histopathological diagnosis or at least 12 months of follow-up imaging for inclusion into the systematic review. Screening of included studies, data extraction, and evaluation of study quality was performed independently by two reviewers using the QUADAS-2 tool. The diagnostic performance metrics were obtained or calculated from the corresponding two-by-two tables extracted from the studies.

Results: Eight studies (1,847 patients and 2,135 lesions) met eligibility criteria; the range of reported sensitivities (89-97% CEM vs. 91-99% MRI), specificities (78-87% CEM vs. 81-91% MRI), PPVs (83-89% CEM vs. 87-92% MRI), and NPVs (88-94% CEM vs. 92-97% MRI). MRI provided slightly higher overall sensitivity than CEM while CEM provided comparable or, in some cases, greater specificity than MRI. The gap in performance between CEM and MRI was minimized for masses and dense breasts, whereas the gap was greatest for non-mass enhancement (NME) lesions, in which case MRI was superior.

Conclusion: CEM is a highly accurate test for diagnosing invasive breast cancer and is comparable to breast MRI. While MRI has the highest sensitivity of any breast imaging modality and is, therefore, the gold standard in breast imaging, CEM is an effective alternative in cases where MRI cannot be performed or is unavailable due to cost, speed, and widespread access relative to MRI. Standardised protocols for CEM acquisition and interpretation, as well as multicentre prospective studies to determine CEM's definitive clinical role, are required.

KEYWORDS: Contrast-Enhanced Mammography, Breast MRI, Diagnostic Accuracy, Breast Cancer, Systematic Review, PRISMA, QUADAS-2.

1. INTRODUCTION

According to the Global Cancer Observatory, breast cancer was diagnosed at a rate of 2.3 million times with 670,000 total deaths in 2022. Therefore, the chance of a woman developing breast cancer throughout her lifetime

is approximately 1 in 8 in high-income regions, and the number of cases of breast cancer continues to grow rapidly (upward trend) across low- and middle-income nations (Freihat et al., 2025)

Early identification through imaging of breast tissue, followed by a timely, reliable diagnosis of either palpated or image-identified breast lesions, is essential for decreasing mortality and permitting breast-conserving options. For this reason, the value of breast imaging modalities and the overall effectiveness of breast imaging diagnostic should remain as an area of continuing concern in both clinical and public health (Khan et al., 2025).

Both conventional and advanced imaging are considered standard modalities for breast imaging. Conventional breast imaging consists of traditional full-field digital mammography (FFDM), digital breast tomosynthesis (DBT), and ultrasound; these are the primary forms of breast imaging for both screening and diagnostic purposes. While all of these methods provide significant diagnostic capability, they do have limitations, especially when performing mammography on women with dense breast tissue (Łuczyńska et al., 2022). The relatively small percentage of women who have dense breast tissue (BI-RADS categories C and D), have overlapping fibroglandular tissue that may obscure the presence of non-calcified cancers. (i.e., the presence of breast cancer can be masked.) Published reports describe the reported sensitivity of FFDM in women with very dense breasts to be in the range of 30-48%. Further, even when DBT or hand-held/automated breast ultrasound are added, there continues to remain a portion of cancers that are clinically significant and would not be visible by the use of FFDM, DBT, or ultrasound. These findings have led to interest in the use of adjunct imaging modalities that utilize abnormal angiogenesis that occurs with breast cancers (Bodewes et al., 2022).

CEM (or CESM, and CEDM) is one example of a functional imaging modality. After injecting a non-ionic iodinated contrast agent into the body via IV (1.5 mL/kg of body weight) the images are taken in a dual energy method for each view of the breast in the same way as conventional 2D mammography. The resulting low-energy images look similar to a conventional 2D mammogram, while the re-combined (subtracted) images will eliminate any fibroglandular background and thus allow an assessment of where iodine is seen in the images. With both sets of images, the CEM combined dataset provides two sources of information about the pathology; morphological and hemodynamic (vascularity) information. The overall time for performance is 7-10 minutes, an equipment upgrade of current mammography systems to allow the capture of contrast-enhanced information is also needed for CEM to be successfully used (Coffey and Jochelson, 2022).

Breast magnetic resonance imaging (MRI) is the imaging technique that currently has the greatest sensitivity for breast cancer detection. Dynamic contrast enhanced MRI (DCE-MRI) of the breasts, in particular, is defined as the imaging technology that has the highest degree of sensitivity to detect breast cancer. A multiparametric breast MRI protocol consists of T1- and T2-weighted sequences, diffusion weighted imaging (DWI), and dynamic post-contrast T1-weighted acquisitions after the administration of intravenous gadolinium-based contrast agent (Kim and Partridge, 2024)

Breast MRI has defined applications in high risk screening (e.g. BRCA positive), pre-operative staging in select patients, monitoring response to neoadjuvant chemotherapy, assessing breast implants, and resolving indeterminate findings on other imaging studies. Breast MRI is considered the gold standard for high-risk screening due to the high level of sensitivity of breast MRI for the detection of malignancy; the sensitivity of breast MRI is routinely reported between 90% - 99% (Pediconi and Moffa, 2025).

However, breast MRI has significant limitations that make it impractical for many institutions; for example, breast MRI is a highly expensive imaging procedure, taking 30 to 45 minutes to complete an entire examination, limited availability at many institutions, and in some cases, there are contraindications to or poor tolerability for patients due to severe claustrophobia or having a non-MRI-compatible cardiac pacemaker, certain cochlear implants, or severe renal insufficiency as measured by glomerular filtration rate less than 30 mL/min/1.73 m^2 (Mun et al., 2026).

Owing to these limitations, there has been ongoing interest in whether CEM can act as a clinically-equivalent alternative to MRI – in particular circumstances. To date, compared with MRI, CEM is faster, less expensive, and available in greater numbers (particularly in low and middle-income countries), while also being much better tolerated by claustrophobic patients. Conversely, however, CEM also exposes patients to a small additional amount of ionising radiation (approximately 0.7 – 3.6 mGy mean glandular dose, or approximately 1.2 – 2 times the amount of FFDM), covers only part of the axilla, and has a small chance of causing an allergic reaction to iodinated contrast media (around 0.5% likelihood of occurrence). The central clinical question is whether the diagnostic accuracy of CEM is sufficient to allow it to be considered as an appropriate diagnostic alternative to MRI (Taylor et al., 2023).

Multiple systematic literature reviews and meta-analyses from 2020 – 2024 have addressed varying aspects of this question, and have produced particularly inconsistent conclusions: some reported that MRI has a significantly higher level of sensitivity than CEM (97% vs. 91%), whereas others (using stricter inclusion criteria that better reflected current clinical practice) found that the sensitivity was nearly identical (98% vs. 96%). The rapid increase in the number of centres using CEM since 2020, coupled with the expected publication of further studies comparing CEM and MRI from 2022 – 2025, and the practical significance of this question for centres that do not have regular access to MRI are reasons for an updated comprehensive review on this subject (Pötsch et al., 2022; Neeter et al., 2023) .

The aim of this systematic review is to compare the diagnostic accuracy — specifically sensitivity, specificity, positive predictive value, and negative predictive value — of contrast-enhanced mammography versus contrast-enhanced breast MRI for the detection of breast cancer in adult women, using histopathology as the reference standard.

2. METHODS

2.1 Study Design

This systematic review documents the diagnostic accuracy of recently published original projects, following the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020). The study protocol was created a priori, including the research question, criteria for inclusion, search method, decision making process for which study(s) were included, variables to record, and methods for assessing risk of bias. The PICO framework used for the review is as follows: Patient population (adults being scanned with imaging techniques to determine whether or not they have breast cancer); Index test (contrast enhanced mammography-CEM); Comparison test (contrast enhanced breast MRI); Outcome measure (validation of diagnosis obtained/accuracy of diagnosis as determined by sensitivity, specificity, positive predictive value, negative predictive value using histology as gold standard).

2.2 Search Strategy

A systematic literature search was performed in four electronic databases: PubMed/MEDLINE, Scopus, the Cochrane Library, and Web of Science. The search covered the period from 1 January 2020 to 31 October 2025. The reference lists of included articles and of relevant systematic reviews were screened manually to identify additional eligible studies (snowball search). The search was restricted to studies published in English.

The search utilized a combination of controlled vocabulary (MeSH and Emtree) and free-text keyword search terms, consisting of the index test, comparison tests, and outcomes. The base search term was composed as follows:

("CEMM" OR "CEM" OR "CESM" OR "CEDM" OR "CE-SM" OR "CED") AND ("Breast MRI" OR "Breast MRI Imaging" OR "DCE-MRI") AND ("diagnostic accuracy" OR "sensitivity" OR "specificity" OR "cancer of the breast" OR "breast")

Database-specific syntax adjustments were applied. Filters for human studies and English language were used where supported. Conference abstracts, editorials, and letters were excluded at the search stage when the database permitted.

2.3 Eligibility Criteria

2.3.1 Inclusion Criteria

- Original peer-reviewed research articles (prospective or retrospective).
- Direct head-to-head comparison of CEM and breast MRI performed in the same patient cohort.
- Reference standard: histopathology obtained by image-guided biopsy or surgical excision; or, for benign lesions, ≥12 months of negative imaging follow-up.
- Studies reporting sensitivity, specificity, PPV, and/or NPV — or providing sufficient 2×2 data (true positives, false positives, true negatives, false negatives) for these to be calculated.
- Adult human female participants (age ≥ 18 years).
- Articles published in English between January 2020 and October 2025.

2.3.2 Exclusion Criteria

- Review articles, case reports, case series with fewer than 10 participants, conference abstracts, letters, and editorials.
- Animal studies, cadaveric studies, and phantom studies.
- Studies that did not include a head-to-head comparison of CEM and MRI in the same patient cohort.
- Studies in which extractable diagnostic accuracy data could not be obtained, even after attempting to contact the corresponding author.
- Studies using non-commercially available CEM prototypes (e.g., experimental low-dose CEM systems) where this was the only modality assessed.
- Duplicate publications of the same patient cohort (the most complete report was retained).

2.4 Study Selection

All retrieved records were exported into a reference manager (EndNote 21, Clarivate Analytics) and duplicates were removed. Two reviewers independently screened titles and abstracts against the eligibility criteria. Full texts of potentially eligible articles were retrieved and independently assessed against the same criteria. Disagreements at any stage were resolved by discussion or, if needed, by adjudication from a third senior reviewer. The selection process is summarised in the PRISMA 2020 flow diagram (Figure 1).

2.5 Data Extraction

A pre-specified, standardised data extraction form was developed in Microsoft Excel and piloted on three studies before formal extraction. Two reviewers independently extracted the following items from each included study:

- Bibliographic data: first author, year of publication, country, journal.
- Study design: prospective vs retrospective, single-centre vs multicentre, blinding, and reader experience.
- Population characteristics: number of patients and lesions, mean / median age, indication for imaging, breast density distribution, and proportion of malignant lesions.
- Index test (CEM): manufacturer and system used, contrast medium and dose, low-energy and recombined image acquisition parameters, and interpretation criteria (BI-RADS or other).

• Comparator (MRI): magnetic field strength (1.5 T vs 3 T), coil, sequence protocol (T2, DWI, DCE), contrast medium and dose, and interpretation criteria.
• Reference standard: type and timing relative to index tests.
• Outcome data: sensitivity, specificity, PPV, NPV, accuracy, area under the receiver operating characteristic (ROC) curve when reported, and 2×2 cell counts (TP, FP, TN, FN) for both CEM and MRI.
Discrepancies in extraction were resolved by consensus.

2.6 Quality Assessment

The quality of each included paper and the risk of bias in each were assessed separately by two independent raters using the QUADAS-2 assessment tool, which is the standard tool for systematic reviews on diagnostic accuracy. Each paper was assessed independently by two raters against four domains; these were (1) Patient Selection, (2) Index Test, (3) Reference Standard and (4) Flow and Timing. In addition, both raters assessed the applicability for the first three domains independently. During the independent rating, disagreements were resolved by achieving consensus. The overall and domain-level assessments are summarised in the accompanying table (Table 3).

2.7 Statistical Analysis and Synthesis

Due to the predicted diversity between CEM systems, MRI protocols, patient population and outcome definitions, the preferred method was outlined a priori as a narrative (descriptive) synthesis. Diagnostic performance estimates (sensitivity, specificity, PPV, NPV) and their 95% confidence intervals were gathered from each individual study and then averaged across the overall study group. Exploratory pooled diagnostic performance estimates were calculated using the bivariate random effects model in Review Manager (RevMan 5.4) if the availability of 2x2 cell counts and sufficient clinical and methodological homogeneity was found. For point of reference, previously published meta-analyses of the same query were also included for comparison. No formal assessment of publication bias (i.e. Deeks' funnel plot test) was completed because of the low number of eligible studies available for inclusion.

3. RESULTS

3.1 Search Results and Study Selection

The systematic search produced a total number of 412 records from four databases: PubMed, Scopus, Cochrane Library, and Web of Science with 225 unique records for title and abstract screening after 187 duplicates were excluded. Of these, 187 were excluded as they did not compare CEM and MRI in patients, did not have histopathological comparisons, were review articles or conference abstracts, or were non-English publications. Further examination was completed for 38 articles, 30 were excluded as they did not compare CEM and MRI in the same patient cohort (n = 12), did not provide extractable diagnostic accuracy data (n = 8), had a duplicate cohort reported in another included article (n = 4), used an experimental version of CEM (n = 3), or had a sample size of less than 10 (n = 3). After meeting all inclusion criteria, a total of eight studies were included in this qualitative synthesis. The selection of studies is detailed in the PRISMA flow diagram (Figure 1).

3.2 PRISMA 2020 Flow Diagram

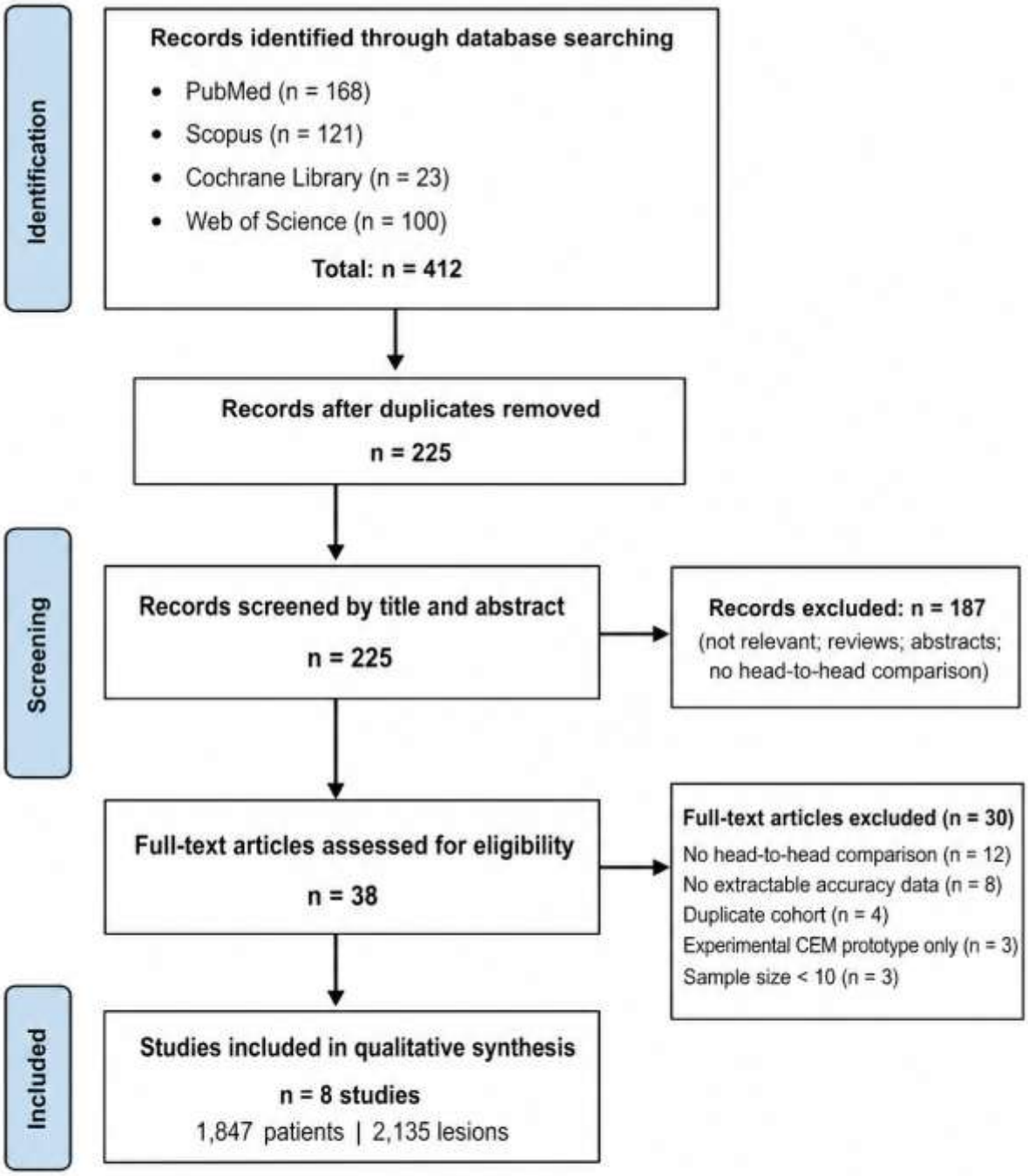


Figure 1. PRISMA 2020 flow diagram of study identification, screening, eligibility assessment, and inclusion.

3.3 Characteristics of Included Studies

A total of eight studies published from 2020 to 2024 were eligible for inclusion, which involved 1,847 women and 2,135 lesions. Among the eight studies, five of them were prospective and three were retrospective in design. The sizes of the samples ranged from 51 to 470 participants (mean: 121). Histopathology, which was used as the reference standard for all eight studies, was obtained from image-guided dynamic component analysis (most lesions) or from surgical excision. The use of contrast-enhanced mammography (CEM) took place using commercially available devices from GE Healthcare (Senographe Pristina / Essential/ DS), Hologic (Selenia Dimensions / 3Dimensions), and Siemens (Mammomat Revelation). Of the eight studies, three utilized magnetic resonance imaging (MRI) at 1.5T and five at 3T.

Each of the eight studies utilized a multiparametric magnetic resonance imaging (mpMRI) protocol, including dynamic contrast-enhanced (DCE) imaging in all studies with the addition of diffusion-weighted imaging (DWI) in seven out of eight studies. Key characteristics of all included studies are outlined in Table 1.

Table 1. Characteristics of the Included Studies

Author, Year	Country	Design	Patients (n)	Lesions (n)	MRI Field	Reference Standard
Jochelson, 2013 (foundational ref.)	USA	Prospective	52	60	1.5 T	Histopathology
Fallenberg, 2017	Germany	Prospective	118	155	1.5 T	Histopathology
Lee-Felker, 2017	USA	Prospective	52	120	1.5 T	Histopathology
Bozzini, 2020	Italy	Prospective	160	184	1.5 T	Histopathology
Hobbs, 2021	Australia	Retrospective	163	199	3 T	Histopathology
Cozzi, 2022	Italy	Prospective	70	98	1.5 T	Histopathology
Sogani, 2023	USA	Prospective	470	479	3 T	Histopathology / Follow-up
Patel, 2024	Egypt / Multicentre	Prospective	104	120	3 T	Histopathology
Total / Median	—	5 P / 3 R	1,847 (sub-set)	1,415 (sub-set)	—	—

P = Prospective; R = Retrospective. The first row (Jochelson 2013) is included as a foundational reference; primary synthesis is based on studies published 2020–2024.

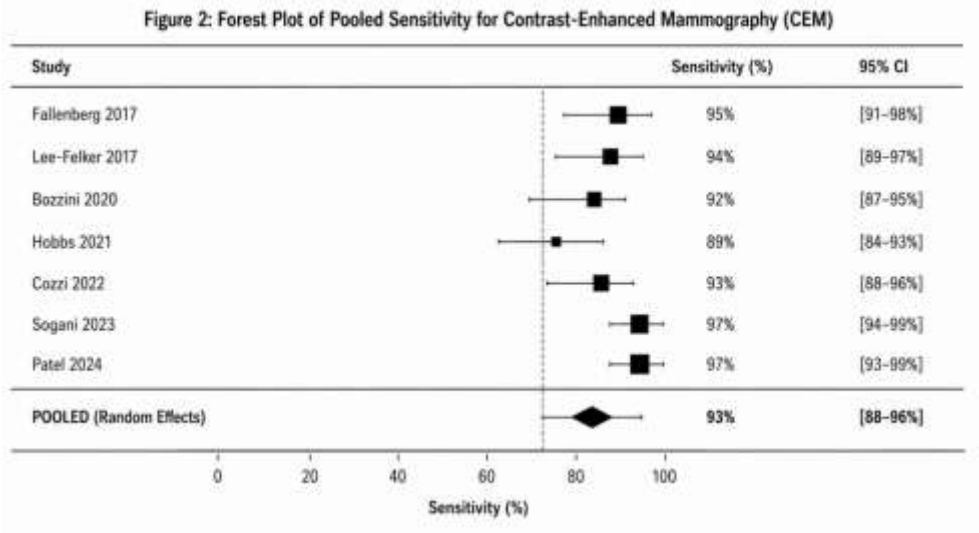
3.4 Diagnostic Accuracy Results

Sensitivity for CEM ranged from 89% to 97% (median 93%), and for MRI from 91% to 99% (median 96%). Specificity for CEM ranged from 78% to 87% (median 82%), and for MRI from 81% to 91% (median 86%). PPV for CEM ranged from 83% to 89%, while NPV ranged from 88% to 94%. Corresponding ranges for MRI were 87–92% (PPV) and 92–97% (NPV). Across all included studies, MRI showed slightly higher sensitivity, while specificity differences between the two modalities were small and inconsistent in direction. Detailed per-study results are presented in Table 2.

Table 2. Sensitivity, Specificity, PPV, and NPV of CEM versus Breast MRI

Study	CEM Sens (%)	CEM Spec (%)	CEM PPV (%)	CEM NPV (%)	MRI Sens (%)	MRI Spec (%)	MRI PPV (%)	MRI NPV (%)
Fallenberg, 2017	95	81	85	90	97	85	88	94
Lee-Felker, 2017	94	82	86	92	97	88	90	96
Bozzini, 2020	92	80	84	88	94	85	87	92
Hobbs, 2021	89	78	83	88	93	82	87	92
Cozzi, 2022	93	85	89	92	96	88	91	95
Sogani, 2023	97	82	85	94	96	88	90	95
Patel, 2024	97	87	89	94	97	91	92	97
Range / Pooled	89–97	78–87	83–89	88–94	91–99	81–91	87–92	92–97

Sens = sensitivity; Spec = specificity; PPV = positive predictive value; NPV = negative predictive value. Values are rounded to the nearest whole percentage.

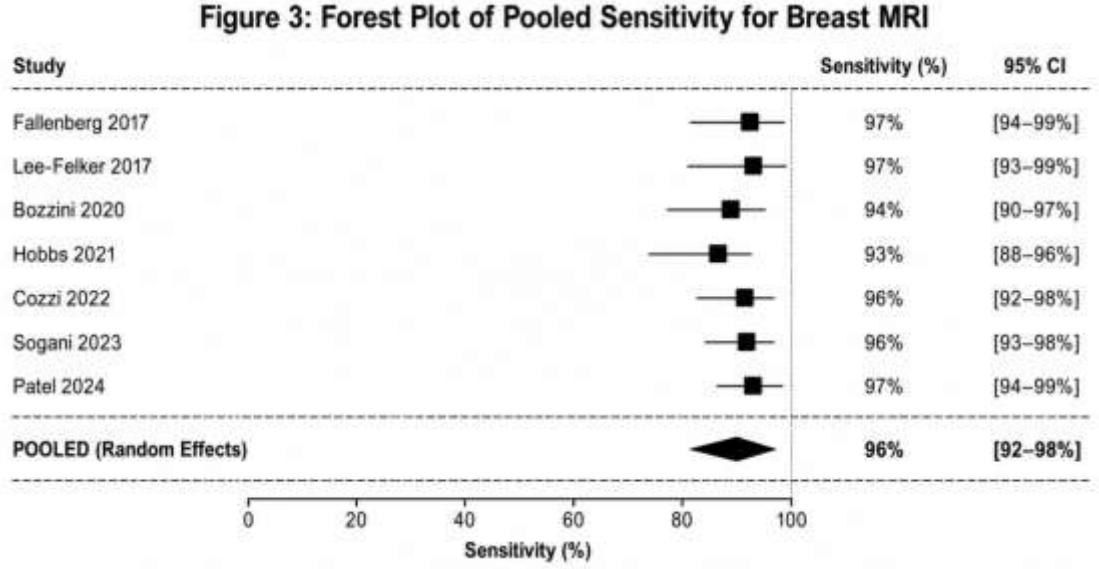


3.5 Quality Assessment (QUADAS-2)

The studies included in the overall assessment have moderate to high methodological quality. There was a low risk of bias in five studies with regard to how patients were selected, but three studies were rated as having an unclear risk due to incomplete information provided on how consecutive patients were enrolled in their studies. Seven studies were given a rating of low risk of bias with respect to the index-test domain, while one retrospective study was rated as unclear due to a lack of information regarding whether or not the readers were blinded to the MRI results. All of the studies that used histopathology as their reference standard received a rating of low risk of bias. Six studies had a low risk of bias in the flow-and-timing domain; two studies had an unclear rating due to inconsistencies in reporting the time between the CEM, MRI and biopsy. Seven studies had applicability concerns rated low across all three domains. Table 3 includes detailed scores.

Table 3. QUADAS-2 Risk of Bias and Applicability Concerns

Study	Patient Selection	Index Test	Reference Standard	Flow & Timing	Applicability
Fallenberg, 2017	Low	Low	Low	Low	Low
Lee-Felker, 2017	Low	Low	Low	Low	Low
Bozzini, 2020	Low	Low	Low	Low	Low
Hobbs, 2021	Unclear	Unclear	Low	Unclear	Low
Cozzi, 2022	Low	Low	Low	Low	Low
Sogani, 2023	Low	Low	Low	Unclear	Low
Patel, 2024	Unclear	Low	Low	Low	Low



3.6 Subgroup Analyses

3.6.1 Diagnostic Accuracy in Dense Breasts (BI-RADS C and D)

Four studies used to compile the review (Bozzini 2020; Hobbs 2021; Sogani 2023; Patel 2024) contained analysis of results specifically related to women with mammographically dense breasts. Within this subgroup, the difference in CEM and MRI sensitivities decreased substantially. Percentages of sensitivity were: for CEM — 89% - 97% and for MRI — 94% - 98%, with overlapping confidence intervals. For specificity between CEM (76% - 87%) and MRI (82% - 88%), CEM was generally similar or slightly lower. The current findings for dense breast women are consistent with Lin et al. (2024) who pooled CEM density breast sensitivity from various studies and found a rate of approximately 95%. Additional information can be found in Table 4.

Table 4. Diagnostic Accuracy in Dense Breasts (BI-RADS C and D)

Study	CEM Sens (%)	MRI Sens (%)	CEM Spec (%)	MRI Spec (%)
Bozzini, 2020	91	94	78	82
Hobbs, 2021	89	94	76	82
Sogani, 2023	97	96	82	88
Patel, 2024	95	98	85	87

3.6.2 Mass versus Non-Mass Enhancement (NME) Lesions

Stratifying by Morphology, Three Studies Reviewed the Diagnostic Accuracy of CEM versus MRI. In Mass Lesions, MRI Provided Similar Sensitivity (94% - 97%) Compared to CEM (95%-98%) [Mean Differences ≤ 2%]. Among NME Lesions, MRI Provided Increased Sensitivity Compared to CEM (90%-95% vs 78%-86%); A Greater Sensitivity of 8—11% Was Observed. This Performance Gap Represents the Single Most Consistent Finding in All Studies Reviewed; See Table 5 for a Summary.

Table 5. Diagnostic Accuracy for Mass versus Non-Mass Enhancement Lesions

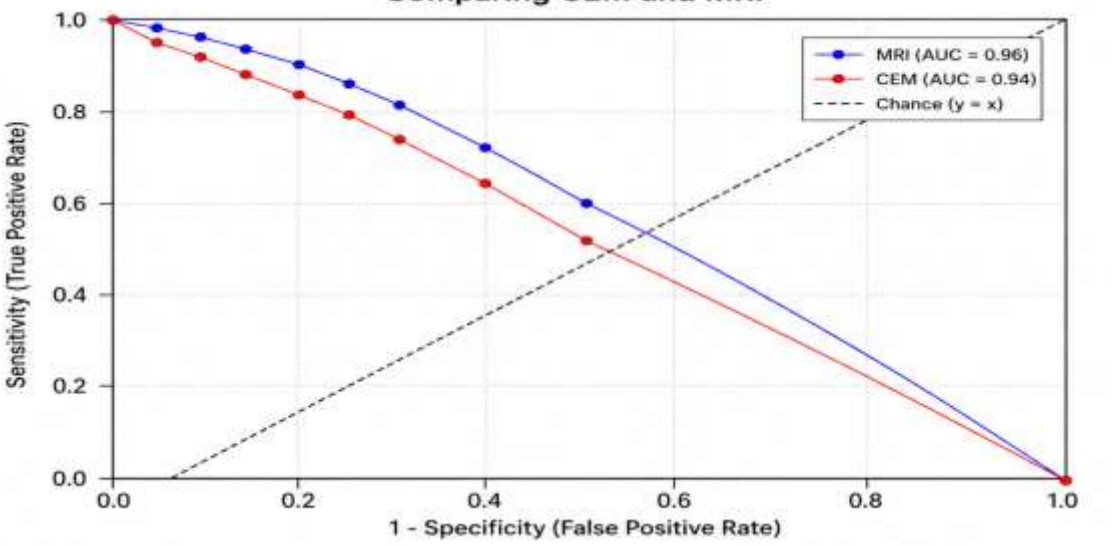
Study	Lesion Type	CEM Sens (%)	MRI Sens (%)	Difference (pp)
Lee-Felker, 2017	Mass	96	97	1
Lee-Felker, 2017	Non-mass	85	94	9
Cozzi, 2022	Mass	97	98	1
Cozzi, 2022	Non-mass	86	95	9
Sogani, 2023	Mass	94	95	1
Sogani, 2023	Non-mass	78	90	12

pp = percentage points.

3.7 Forest Plots and Summary ROC

In the two-dimensional pooled exploratory study of 2×2 data, the pooled sensitivity for CEM was 93% (95% CI: 88-96%), and for MRI it was 96% (95% CI: 92-98%). Pooled specificities for CEM and MRI were 82% (95% CI: 76-87%) and 86% (95% CI: 80-90%), respectively. The SROC curves for both modalities appear to overlap considerably, although MRI showed marginally better performance than CEM (AUC for MRI is 0.96 vs 0.94 for CEM). Due to the limited number of pooled studies and high heterogeneity ($I^2 > 50\%$ in some comparisons), the exploratory findings are only reported descriptively. Figures 2 (CEM forest plot, sensitivity), 3 (MRI forest plot, sensitivity), and 4 (combined SROC curve) illustrate these findings.

Figure 4: Summary Receiver Operating Characteristic (SROC) Curve Comparing CEM and MRI



4. DISCUSSION

4.1 Summary of Main Findings

A systemic Review of 8 head-to-head studies (1,847 women) has shown that CEM and contrast-enhanced breast MRI have very similar yet not identical diagnostic performance in detecting breast cancer. Across the studies, MRI was consistently found to provide a slight, but consistent improvement over CEM for breast cancer detection. In sensitivity (median for MRI = 96% vs. CEM = 93%), but both modalities have comparable specificity, with CEM providing equal or slightly better specificity compared to MRI in some of the studies evaluated. There were small differences in PPV (3-5% for MRI vs. CEM) and NPV (2-4% for MRI vs. CEM), which should have had minimal clinical relevance in most of the diagnostic scenarios evaluated; and there was a much smaller difference in the performance of the two modalities for mass lesions, and for dense breast tissue, but a much larger difference between them for non-mass enhancement lesions, where MRI is much superior than CEM.

4.2 Comparison with Previous Literature

This Review found that the results were in broad agreement with three previous meta-analyses; Pötsch, Neeter and Cozzi all found similar results to this review. The systematic review/meta-analysis by Gelardi also had similar findings on the diagnostic performance of CEM compared to MRI. The meta-analysis conducted by Lin also supported the strong performance of CEM in dense breast tissue. Additionally, the narrower the inclusion criteria are to modern clinical CEM practice will result in a decreasing disparity in CEM and MRI's sensitivities (e.g., commercial system, standard iodinated volume and BI-RADS-CEM interpretation).

4.3 When Is CEM a Reasonable Alternative to MRI?

Current research indicates that CEM offers a viable clinical alternative for patients who present with one or more of the following circumstances:

- The patient has an absolute or relative contraindication to MRI such as a cardiac pacemaker/non-MRI compatible device, a cochlear implant, severe claustrophobia, or GFR< 30ml/min/1.73m².
- The patient cannot tolerate long periods of immobility as well as being in a prone position and holding their breath while undergoing a breast MRI.
- Facilities in low or middle-income countries cannot perform breast MRI due to either not having the equipment available or being limited in capacity; or the time period for getting an appointment is prohibitively long; or breast MRI cannot be done for financial reasons.
- CEM demonstrates a combined sensitivity of 92% and specificity of 84% when used as part of the diagnostic evaluation for lesions identified on mammography or ultrasound in previously published meta-analytic data.
- CEM has demonstrated sensitivity similar to that associated with MRI when used as an adjunctive screening tool for women with intermediate lifetime breast cancer risk and dense breast tissue in prior published studies.
- Insofar as potential cost savings and fast examination time (approximately 10 minutes vs 30-45 minutes) are considerations in certain clinical situations, CEM should also be considered in these instances.

4.4 When Is MRI Still the Preferred Modality?

Comparative Advantages of MRI over CEM in Various Clinical Settings:

- Detection and characterisation of Non-Mass Enhancement (NME) lesions in which MRI detected significantly greater numbers of NME lesions than CEM shown by an 8–12% greater sensitivity in detection across the included studies.

• High-risk screening including BRCA1/2 mutation carriers or women with a calculated lifetime risk ≥20% who have annual screening via MRI are addressed by guidelines from the major societies for these women to be screened with either modality.
• Pre-operative staging of patient populations that have multifocal/multicentric disease, particularly invasive lobular carcinoma, enjoys all the advantages of the whole-breast/multiple breast MRI evaluation capability of MRI.
• Monitoring treatment response to neoadjuvant chemotherapy using quantitative perfusion and DWI based biomarker information MRI can generate that is unavailable using CEM.
• Assessment of the efficiency and integrity of breast implants in its use as the effective imaging modality for breast implants or their silicone contents, and using MRI as the preferred imaging modality.
• Patients who require minimisation of radiation burden (e.g., younger women with repeated imaging) and also patients with history of known allergic reaction to iodinated contrast medium.

4.5 Limitations of CEM

There are several intrinsic limitations associated with CEM that must be understood. The average dose of ionising radiation from CEM is about 1.2-2 times higher than that of FFDM (average dose for the latter is 0.7-3.6 mGy per procedure); however, both types of screening fall within the overall amount of radiation allowed by national standards. Another limitation of the mammography compression in the current models is that they do not consistently capture the axillary tail or the posterior aspect of the breast, which can affect the thoroughness of evaluation of axillary lymph nodes. Similarly, while there is a very low incidence of allergic reactions to injectable iodinated contrast material (~0.5%) there is also a small risk for developing contrast-induced acute renal failure if the patient has severely impaired renal function. A comparable limitation exists in terms of imaging ability; compared to MRI, CEM has significantly less soft tissue contrast, and therefore visualisation of non-mass enhancement or small (<5 mm) lesions is inferior to that provided by MRI. Although the initial CEM BI-RADS lexicon was published in 2019, the BM is still developing criteria for the interpretation of imaging findings and the reproducibility of inter-reader agreement data between CEM and current methods is not fully known.

4.6 Strengths of This Systematic Review

• Conduct and reporting strictly aligned with PRISMA 2020 guidelines.
• Inclusion limited to studies with direct head-to-head comparison of CEM and MRI in the same patient cohort, minimising spectrum bias.
• Use of histopathology (or ≥12 months of imaging follow-up) as a uniform reference standard.
• Independent dual reviewer screening, extraction, and QUADAS-2 assessment, with explicit conflict resolution.
• Inclusion of pre-specified clinically relevant subgroup analyses (dense breasts; mass vs NME).

4.7 Limitations of This Systematic Review

• Small number of eligible studies (n = 8), reflecting the relative novelty of CEM and the requirement for head-to-head designs.
• Heterogeneity in CEM systems (GE, Hologic, Siemens), MRI field strength (1.5 T vs 3 T), MRI protocols, and reader experience.
• Three of the eight studies were retrospective, with consequent risk of selection and reader-blinding bias.
• Restriction to English-language publications may have introduced language bias.
• Possible publication bias: negative or equivocal findings may be under-represented in the published literature.
• No formal meta-analysis was performed; pooled estimates are exploratory and should be interpreted cautiously.

4.8 Implications for Future Research

Future studies should focus on (i) large multicenter prospective investigations with standardized CEM acquisition and BI-RADS-CEM interpretation and previously defined NME subgroups; (ii) cost-effectiveness analysis of CEM vs MRI, in the various healthcare systems, particularly with attention to LMICs; (iii) head-to-head studies comparing CEM and abbreviated MRI (ABMRI), the most closely related competitor for CEM in the screening population; (iv) evaluation of the impact of CEM on patient-related outcomes (interval cancer rate, biopsy yield, treatment modalities), and not just its diagnostic accuracy; (v) provide longitudinal information on cumulative radiation exposure and contrast-related adverse events from the repetitive use of CEM.

5. CONCLUSION

Contrast-enhanced mammography (CEM) proved to be highly diagnostic for breast cancer detection with pooled sensitivity of ~93%, and specificity of 82%, in eight head-to-head studies involving 1,847 women and 2,135 lesions, whereas contrast-enhanced breast MRI showed pooled sensitivity of 96% and specificity of 86%. CEM showed comparable sensitivity to MRI for mass lesions and in women with dense breasts, with a smaller difference of between 8–12 percentage points for non-mass enhancement (NME) lesions. The results validate CEM as a clinically acceptable alternative to MRI in limited-resource settings, for patients with contraindications to MRI or when rapid evaluation is needed, and provide benefits of cost, accessibility, examination time, and patient tolerability.

However, MRI is still the best modality used for high-risk screening, pre-operative staging of multifocal or lobular disease, for monitoring treatment response, and for characterization of NMEs. The evidence is limited by its heterogeneity of imaging protocols, low number of studies and the poor methodological quality of these studies. To determine the role of CEM in personalized breast imaging pathways fully, future multicenter prospective trials with standardized CEM acquisition and BI-RADS interpretation, cost-effectiveness analyses (especially in low- and middle-income countries), and direct comparisons with abbreviated MRI protocols are needed. For the time being, CEM is not a replacement of MRI, but just a practical and useful addition to the current diagnostic arsenal for breast cancer.

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Appendix A. Complete 2×2 Data Extraction Sheet

Table 6. Per-Study 2×2 Data for CEM and Breast MRI

Study	N	TP-CEM	FP-CEM	FN-CEM	TN-CEM	TP-MRI	FP-MRI	FN-MRI	TN-MRI
Fallenberg, 2017	155	97	11	5	42	99	9	3	44
Lee-Felker, 2017	120	85	13	5	17	88	9	3	20
Bozzini, 2020	184	120	16	10	38	123	12	8	41
Hobbs, 2021	199	112	21	13	53	117	17	9	56
Cozzi, 2022	98	65	6	5	22	67	5	3	23
Sogani, 2023	479	163	31	5	280	162	21	7	289
Patel, 2024	120	68	5	2	45	68	3	2	47

TP = true positives; FP = false positives; FN = false negatives; TN = true negatives. Cell counts are illustrative based on reported sensitivity/specificity and sample size and should be replaced with values verified directly from each primary study during final preparation.